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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,844	01/09/2006	Ashwini Kumar Gupta	V0005.70100US00	1829
23628 7590 06/17/2008 WOLF GREENFIELD & SACKS, P.C. 600 ATLANTIC AVENUE BOSTON, MA 02210-2206				
EXAMINER				
MABRY, JOHN				
ART UNIT		PAPER NUMBER		
1625				
MAIL DATE		DELIVERY MODE		
06/17/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/527,844

Applicant(s)

GUPTA ET AL.

Examiner

John Mabry, PhD

Art Unit

1625

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 March 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 and 26-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 26-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/5508)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Examiner's Response

Applicant's response on March 3, 2008 filed in response to the Office Action dated November 11, 2007 has been received and duly noted.

In view of this response, the status of the rejections/objections of record is as follows:

Status of the Claims

Claims 1-9 and 26-32 are pending and rejected.

Claims 10-25 have been cancelled.

Claims 26-32 are new and rejected.

Claim Objection(s)

The claim objection of claim 12 regarding claim dependency has been overcome in view of Applicants cancelling the claims.

35 USC § 112 Rejection(s)

The 112-2nd rejection of claims 2, 3 and 12 regarding claim lack of antecedent basis has been overcome in view of Applicants cancelling claim 12 and amending claim 2 and 3.

The 112-1st rejection of claims 1-9, 12 and 25 regarding the scope of enablement for R1, R2, R3, R4 and R6, the terms alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, alkylaryl, alkenylaryl, and alkynylaryl which includes heteroatoms in it carbon skeleton have not been overcome in view of Applicants amending the claims.

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Furthermore, the Applicant is not enabled for the scope of the claimed substituents of said variables as well as alkyl.

Examiner has fully considered all of the factors in the determining that the instant application is not enabled for the full scope of the claims.

The breath of the claims is unreasonably broad even in view of the Specification. For example, Applicant claims a tremendous number of possible functional groups and rings structures of variables R1 and R2. It is very well possible that within this claimed process of preparing 2-amino-4,5,6,7-tetrahydro-6-aminobenzothiazoles, these claimed functional groups can be reactive during this process and impede or even not allow the individual steps in the process due to side reactions.

Applicant claims R1 and R2 as follows:

R¹ and R² are independently hydrogen or a C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, C₂-C₁₂ alkynyl, C₄-C₁₄ aryl, (C₄-C₁₄)aryl(C₁-C₁₂)alkyl, (C₄-C₁₄)aryl(C₂-C₁₂)alkenyl, (C₄-C₁₄)aryl(C₂-C₁₂)alkynyl, (C₁-C₁₂)alkyl(C₄-C₁₄)aryl, (C₂-C₁₂)alkenyl(C₄-C₁₄)aryl or (C₂-C₁₂)alkynyl(C₄-C₁₄)aryl group, which may be unsubstituted or substituted with one or more of -F, -Cl, -Br, -I, -CF₃, -C(CH₃)₃, -CH₃, -OH, -SH, -NH₂, -CN, -NO₂, -COOH, -R'-O-R'', -R'-S-R'', -R'-SO-R'', -R'-SO₂-R'', -R'-SO₂-OR'', -R'-O-SO₂-R'', -R'-SO₂-N(R'')₂, -R'-NR''-SO₂-R'', -R'-O-SO₂-N(R'')₂, -R'-NR''-SO₂-OR'', -R'-NR''-SO₂-N(R'')₂, -R'-N(R'')₂, -R'-P(R'')₂, -R'-Si(R'')₃, -R'-CO-R'', -R'-CO-OR'', -R'-O-CO-R'', -R'-CO-N(R'')₂, -R'-NR''-CO-R'', -R'-O-CO-OR'', -R'-O-CO-N(R'')₂, -R'-NR''-CO-N(R'')₂, -R'-CS-R'', -R'-CS-OR'', -R'-O-CS-R'', -R'-CS-N(R'')₂, -R'-NR''-CS-R'', -R'-O-CS-OR'', -R'-O-CS-N(R'')₂, -R'-NR''-CS-OR'', -R'-NR''-CS-N(R'')₂ or -R'', or together with the nitrogen to which they are attached, R¹ and R² form a ring;

and R3 as follows:

R³ is any atom or group, hydrogen or a C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, C₂-C₁₂ alkynyl, C₃-C₁₄ aryl, (C₃-C₁₄)aryl(C₁-C₁₂)alkyl, (C₃-C₁₄)aryl(C₂-C₁₂)alkenyl, (C₃-C₁₄)aryl(C₂-C₁₂)alkynyl, (C₁-C₁₂)alkyl(C₃-C₁₄)aryl, (C₂-C₁₂)alkenyl(C₃-C₁₄)aryl or (C₂-C₁₂)alkynyl(C₃-C₁₄)aryl group, which may be unsubstituted or substituted with one or more of -F, -Cl, -Br, -I, -CF₃, -CCl₃, -CBr₃, -Cl₂, -OH, -SH, -NH₂, -CN, -NO₂, -COOH, -R'-O-R'', -R'-S-R'', -R'-SO₂-R'', -R'-SO₂-N(R'')₂, -R'-SO₂-OR'', -R'-O-SO₂-R'', -R'-SO₂-N(R'')₂, -R'-NR''-SO₂-R'', -R'-O-SO₂-OR'', -R'-O-SO₂-N(R'')₂, -R'-NR''-SO₂-OR'', -R'-NR''-SO₂-N(R'')₂, -R'-N(R'')₃, -R'-N(R'')₂, -R'-P(R'')₃, -R'-Si(R'')₃, -R'-CO-R'', -R'-CO-OR'', -R'-O-CO-R'', -R'-CO-N(R'')₂, -R'-NR''-CO-R'', -R'-O-CO-OR'', -R'-O-CO-N(R'')₂, -R'-NR''-CO-OR'', -R'-NR''-CO-N(R'')₂, -R'-CS-R'', -R'-CS-OR'', -R'-O-CS-R'', -R'-CS-N(R'')₂, -R'-NR''-CS-R'', -R'-O-CS-OR'', -R'-O-CS-N(R'')₂, -R'-NR''-CS-OR'', -R'-NR''-CS-N(R'')₂ or -R'' to yield the 2-amino-4,5,6,7-tetrahydro-6-aminobenzothiazole 5a or an enantiomer or a salt thereof;
wherein -R' is independently a chemical bond, a C₁-C₁₀ alkylene, C₁-C₁₀ alkenylene or C₁-C₁₀ alkynylene group, and -R'' is independently hydrogen, unsubstituted C₁-C₆ alkyl or unsubstituted C₆-C₁₀ aryl.

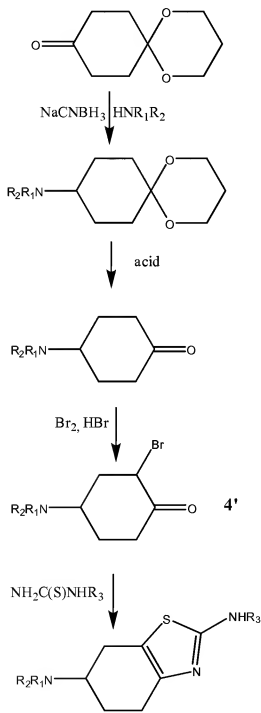
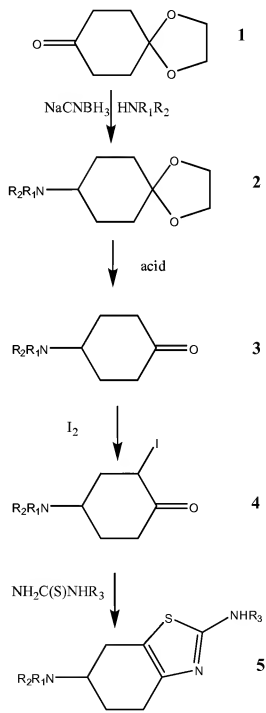
It is not trivial to experimentally interchange any and all of the many substituents that exist. As described by F. Zaragoza Dörwald, most organic syntheses fail initially and chemical research is highly inefficient due to chemists spending most of their time "finding out what went wrong and why". Therefore, most syntheses of organic compounds are labor-intensive and demanding. Additionally, most final synthetic routes to desired organic molecules are usually very different from initially planned routes. A highly skilled chemist can agree that for many successful organic compounds made, many failures are encountered and experimental repetition is common. This also contributes to the undue burden and unpredictability of the syntheses of said compounds. (see "Side Reactions in Organic Synthesis: A Guide to Successful Synthesis Design" 2005 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

Additionally, a key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to a make the invention are available. There is little or no guidance in the Specification for the preparation of such claimed functional groups and ring structures as claimed. That provided is very limited. Applicant shows a general synthesis of compounds of application's general formula I. Pages 11-14 of the Specification describes starting materials and methods for synthesis of compounds wherein R1 and R2=H and n-propyl and R3=H, but does not describe or list any reagents wherein compounds can be used to synthesis compounds where R1, R2, R3, R4 and R6 as listed above. There is limited evidence in the Specification of the example compounds that only covers no or a small portion of the substituents claimed of formula I. Thus, there is no specific direction or guidance regarding said compounds specifically mentioned in Scope. The specification does not provide any support for the synthesis of such claimed compounds a listed above.

35 USC § 103(a) Rejection(s)

Applicant's arguments with respect to 103(a) rejections have been fully considered and are not persuasive. The 103(a) rejection of claims 1-9, 12 and 25 (previous claims) and 1-9 and 26-30 (current claims) regarding obviousness over Leguzza et al (EP 0207696 A1) in view of Solomons et al (Organic Chemistry, 9th Edition, 2008) remains rejected.

Below is a comparison of the process as described by Leguzza (see pages 7-10) versus the Applicant's claimed process:

Leguzzza**Applicant**

These two processes correlate in every aspect with the exception of the step of converting 3 → 4. Leguzza's disclosure converts aminoketone (3) to the alpha-bromoketone (4') then concentrates the crude reaction mixture of (4'). The crude reaction mixture of (4') is then converted to the final product (5).

The instant application claims a process which converts the aminoketone (3) to the alpha-iodoketone (4) *in situ* then converts (4) to the final product (5).

As clearly describes in previous Non-Final Office Action, the instant application is obvious over the process of Leguzza. An artisan of ordinary skill would be motivated to make the alpha-iodoketone (4) in place of the alpha-bromoketone (4') because I⁻ (iodide) is a better leaving group compared to Br⁻ (bromide) as described by Solomons. One of ordinary skill in the art would be further motivated to convert the alpha-haloketone to the desired product (5) to (a) increase the yield and (b) more facile way of achieving the desired product (one less step). Thus, the instant application is rendered obvious over Leguzza in view of Solomons.

Additionally, claims 1-9 and 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leguzza in view of Solomons in references mentioned above. The adjustment of particular conventional working conditions (e.g. determining result effective amounts of the ingredients beneficially taught by the cited references), as well as adjustment of reaction temperature, reaction time and use of solvents, is deemed merely a matter of judicious selection and routine optimization which is well within the

purview of the skilled artisan (*In re* Mostovych, Weber, Mitchell and Aulbach, 144 USPQ 38). Accordingly, these types of modifications would have been well within the purview of the skilled artisan and no more than an effort to optimize results.

The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR* noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Court quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006), stated that “[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR*, 550 U.S. at ___, 82 USPQ2d at 1396. Exemplary rationales that may support a conclusion of obviousness include:

- (A) Combining prior art elements according to known methods to yield predictable results;
- (B) Simple substitution of one known element for another to obtain predictable results;
- (C) Use of known technique to improve similar devices (methods, or products) in the same way;
- (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;
- (E) “Obvious to try” – choosing from a finite number of identified, predictable

solutions, with a reasonable expectation of success;

- (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art;
- (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention. See MPEP § 214.3 for a discussion of the rationales listed above along with examples illustrating how the cited rationales may be used to support a finding of obviousness. See also MPEP § 2144-§2144.09 for additional guidance regarding support for obviousness determinations.

The aforementioned reasons above describe rationales that support a conclusion of obviousness based upon the KSR International Co. v. Teleflex Inc. decision. At least letters (A) - (G) rationale is supported above.

Due to Applicant's amendments, an action on the merits of claims 1-9 and 26-32 is contained herein below.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

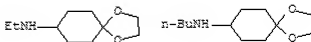
A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 31 is rejected under 35 U.S.C. 102(b) as being anticipated by Yokum et al (Tet. Lett. 1997, 38, 4013-4016).

Yokum discloses compounds of Formula 2a wherein R1=H and R2=ethyl and butyl (see compounds 4a and 4c, page 4014). Thus, said compounds are anticipated by Yokum.



Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

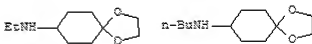
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yokum et al (Tet. Lett. 1997, 38, 4013-4016).

The instant application discloses a compounds of Formula 2a wherein R1=H and R2=propyl.

Scope & Content of Prior Art MPEP 2141.01

Yokum discloses compounds of Formula 2a wherein R1=H and R2=ethyl and butyl (see compounds 4a and 4c, page 4014). Thus, said compounds are anticipated by Yokum.



Differences between Prior Art & the Claims MPEP 2141.02

Yokum differs from the instant application at the R2 position: Yokum's ethyl and butyl versus Applicant's propyl. These are considered homologs.

The MPEP 2144.09 which states: Compounds which are homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH₂- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).

Prima Facie Obviousness, Rational & Motivation MPEP 2142-2413

It would be obvious to one of ordinary skill in the art to make the propyl derivative of 2a as claimed in the instant application over the disclosed compounds of Yokum which discloses the ethyl and butyl derivatives of 2a. Yokum's reference clearly describes one less carbon (ethyl) and one more carbon (butyl) compared to the claimed compound (propyl).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

Claims 1-9 and 26-32 are pending and rejected.

Claims 10-25 have been cancelled.

Claims 26-32 are new and rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John Mabry, PhD whose telephone number is (571) 270-1967. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, PhD, can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/John Mabry/
Examiner
Art Unit 1625

/Rita J. Desai/
Primary Examiner, Art Unit 1625